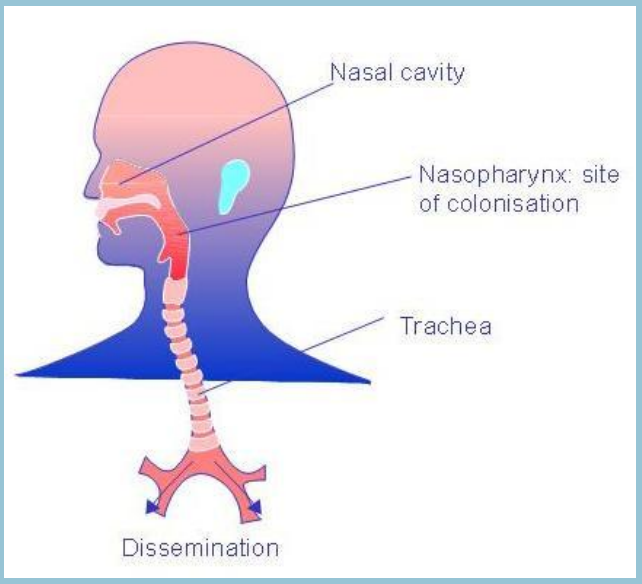
Application of novel technologies to improve access to vaccines in developing countries



Douglas Holtzman
Senior Program Officer
Bill & Melinda Gates Foundation

International Vaccine Technology Workshop
September 18th, Hyderabad India

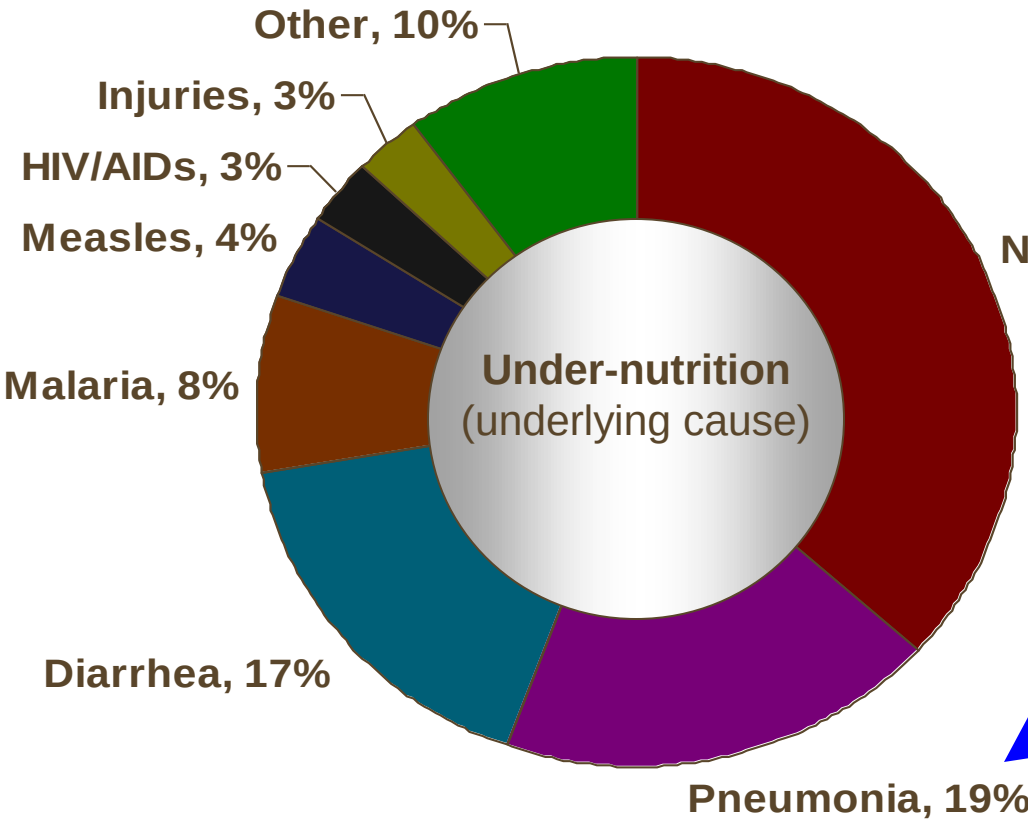
BILL & MELINDA GATES *foundation*

Outline

- Pneumonia, child health and vaccines
- The challenge of seasonal and pandemic influenza

Under 5 Child Mortality

Global Distribution of Cause Specific Child Deaths



Pneumonia – the leading infectious cause of death in children < 5

Source: 2005 World Health Report

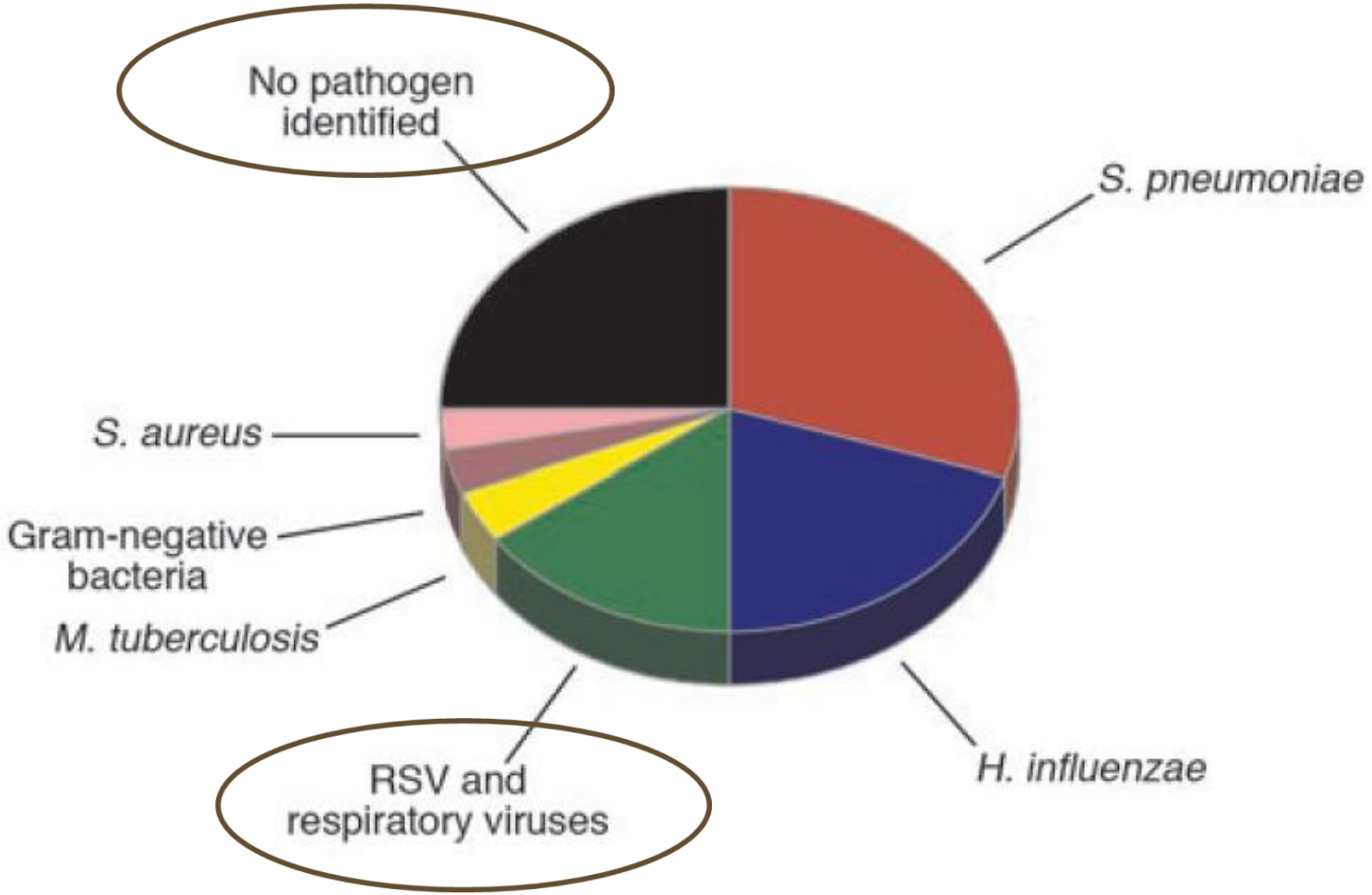
*26% of neonatal deaths are due to severe infections such as pneumonia, meningitis, sepsis/septicaemia, etc

Every year, pneumonia causes nearly two million deaths in children under 5

More than AIDS, malaria and measles combined

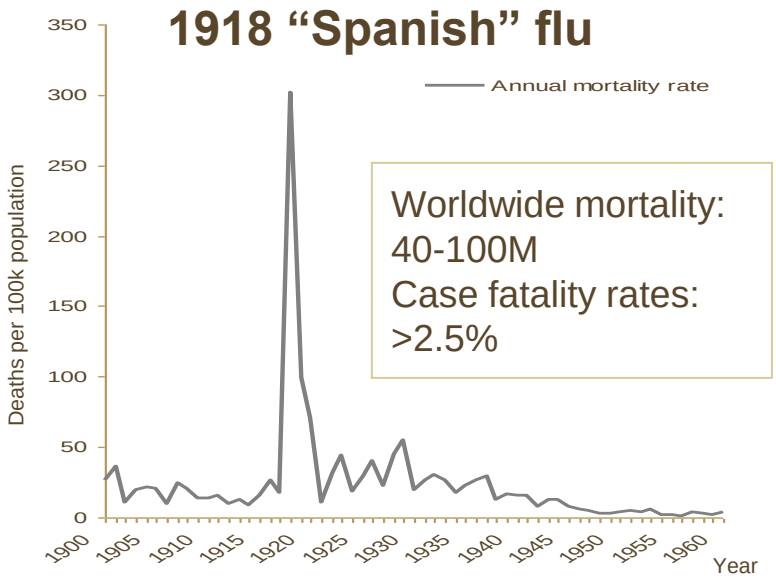
Source: UNICEF, 2006

Microbial Causes of Pneumonia



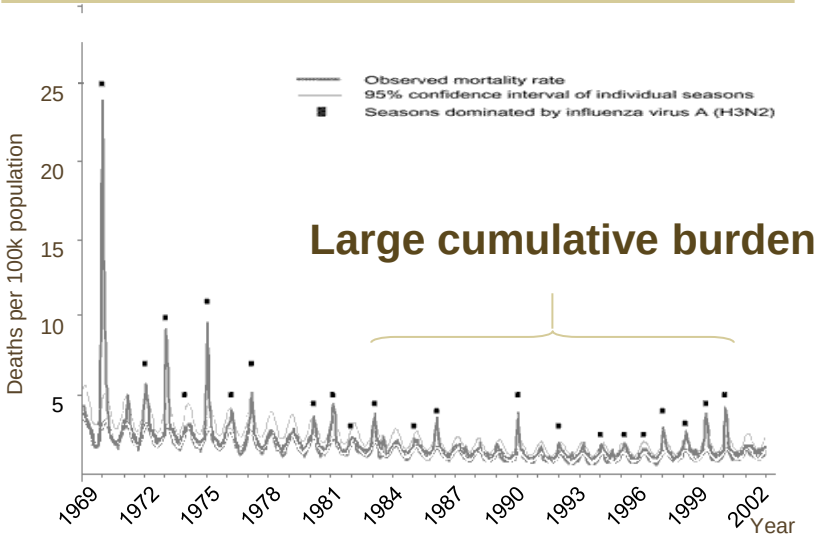
Seasonal and Pandemic Influenza

USA annual influenza mortality, 1900-1960



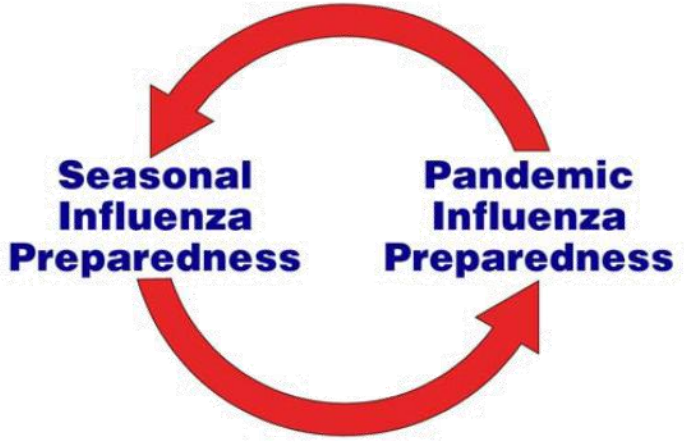
Worldwide mortality:
40-100M
Case fatality rates:
>2.5%

Italy monthly influenza mortality, 1969- 2002



World Health Organization Pandemic Phases

Phases	Phase Description	Level
Inter-Pandemic Phase	Low Risk of Human Cases	1
New Virus in Animals, No Human Cases	Higher Risk of Human Cases	2
Pandemic Alert	No or Very Limited Human-to-Human Transmission	3
New Virus Causes Human Cases	Evidence of Increased Human-to-Human Transmission	4
	Evidence of Significant Human-to-Human Transmission	5
Pandemic	Efficient and Sustained Human-to-Human Transmission	6



CDC National Center for Health statistics

Rizzo, et al., Emerg Infect Diseases (2007)

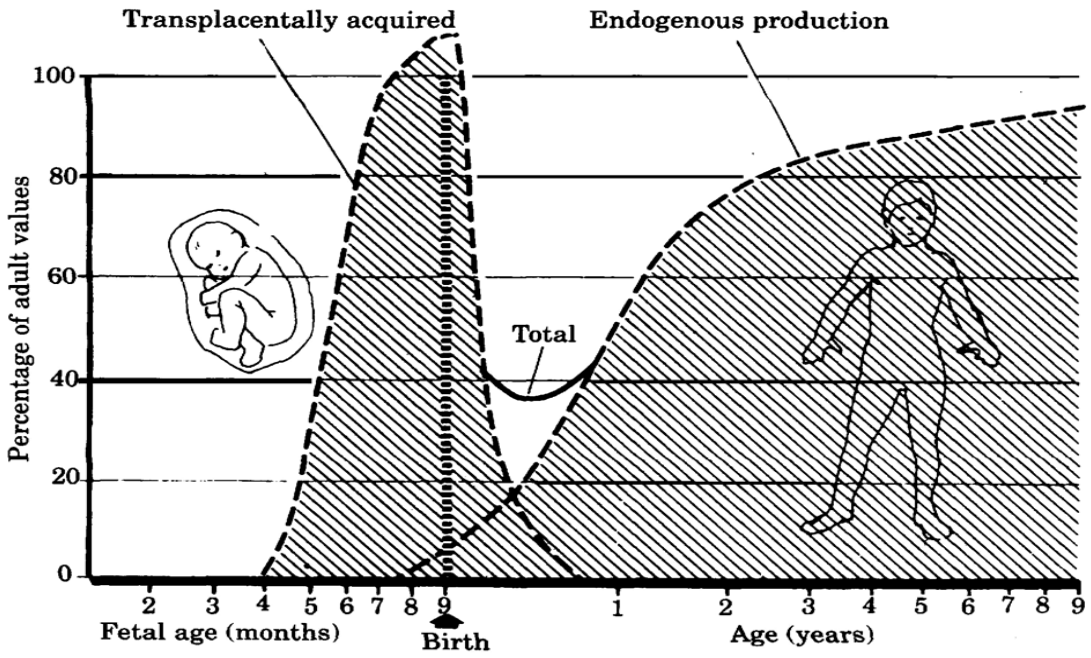
The Challenge:

Capacity for production of seasonal vaccine can not cope with pandemic need therefore:

- **Increase seasonal use**
- **Think ahead of the virus**
- **Increase speed/scale of production through new technologies (multi-use)**

Mother's Gift Study

Immunizing Mothers Prevents Influenza in Infants

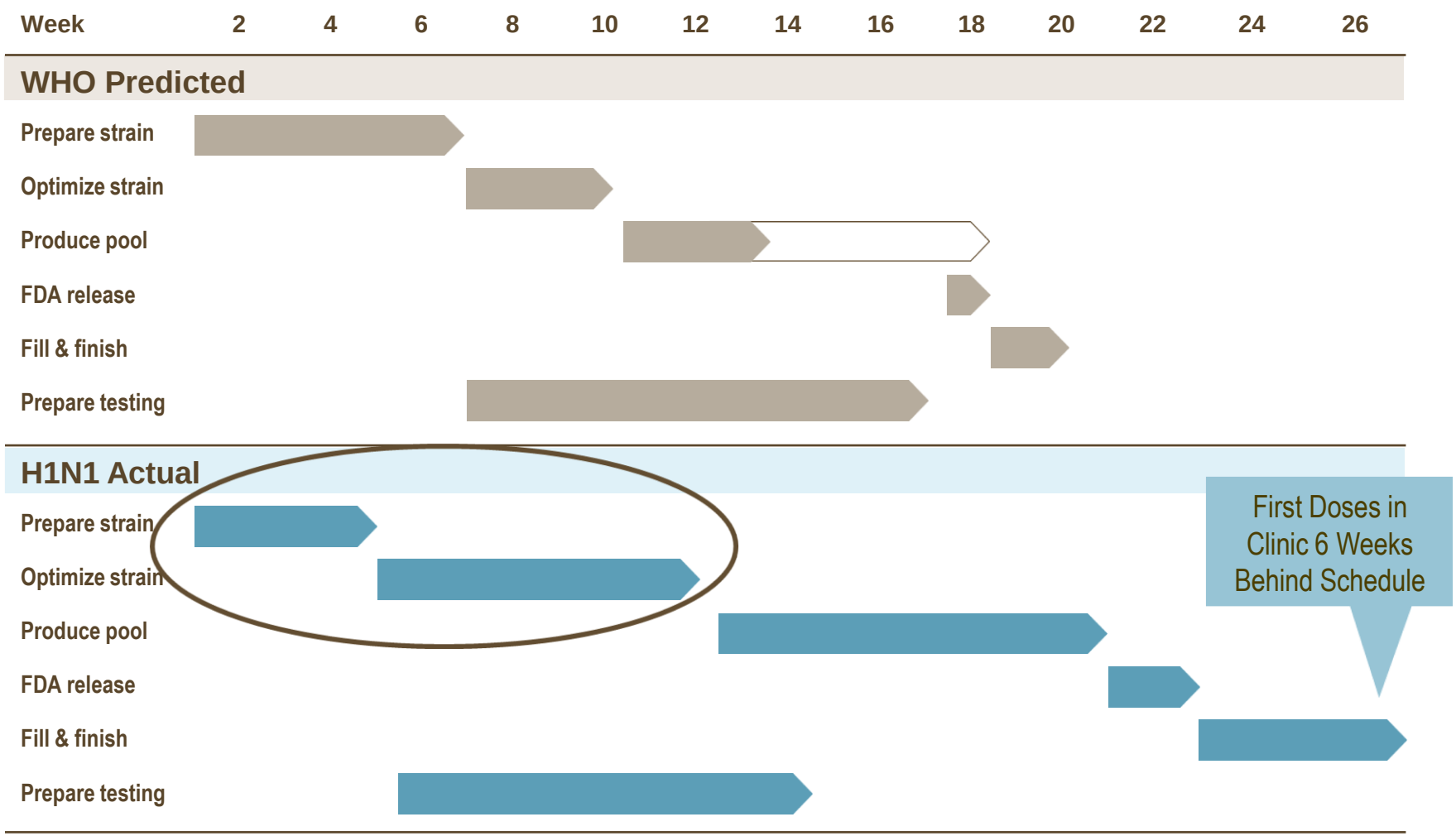


Flu vaccine reduces the rates of respiratory illness with fever

Infants - 34% reduction
Mothers - 63% reduction

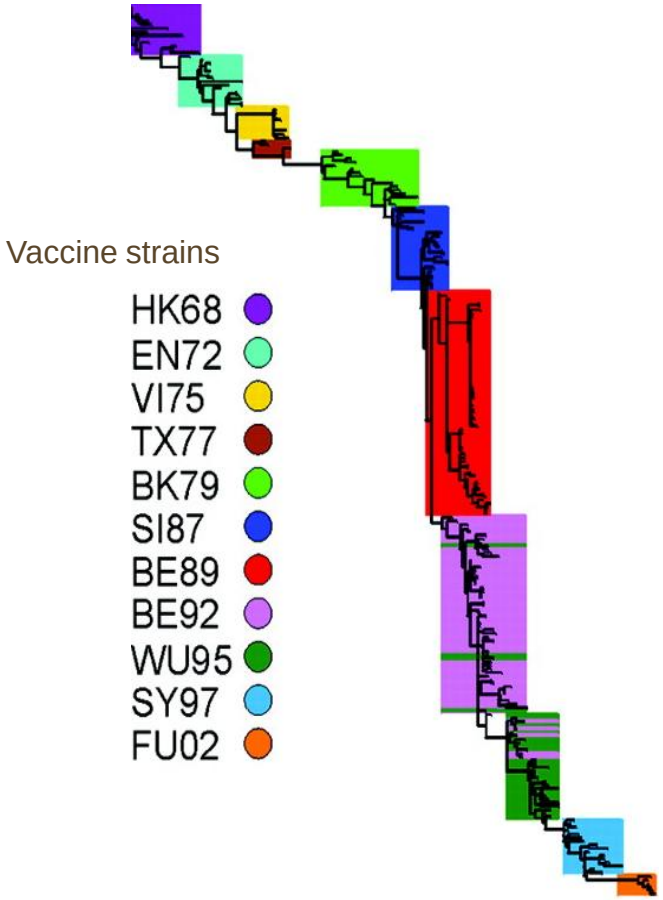
Zaman et al. NEJM 2008 Oct 9;359(15):1555-64

H1N1 Vaccine Production Timeline

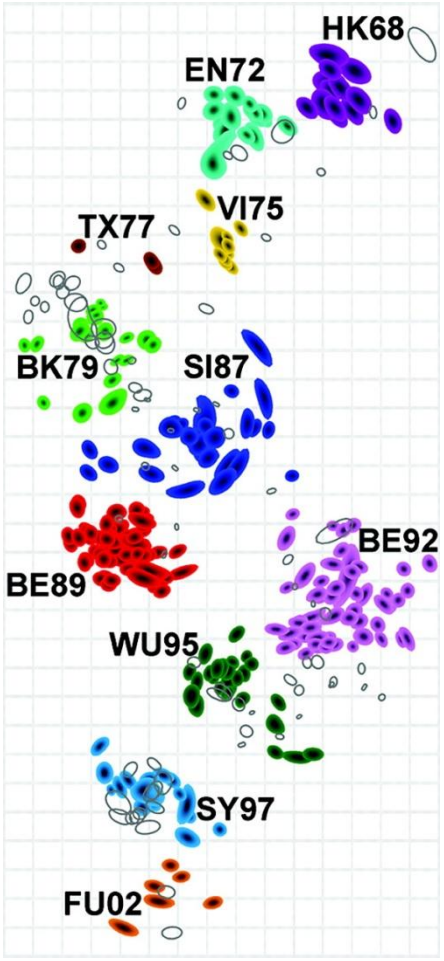


Genetic and Antigenic Evolution of H3N2 HA Sequences

Genetic distance

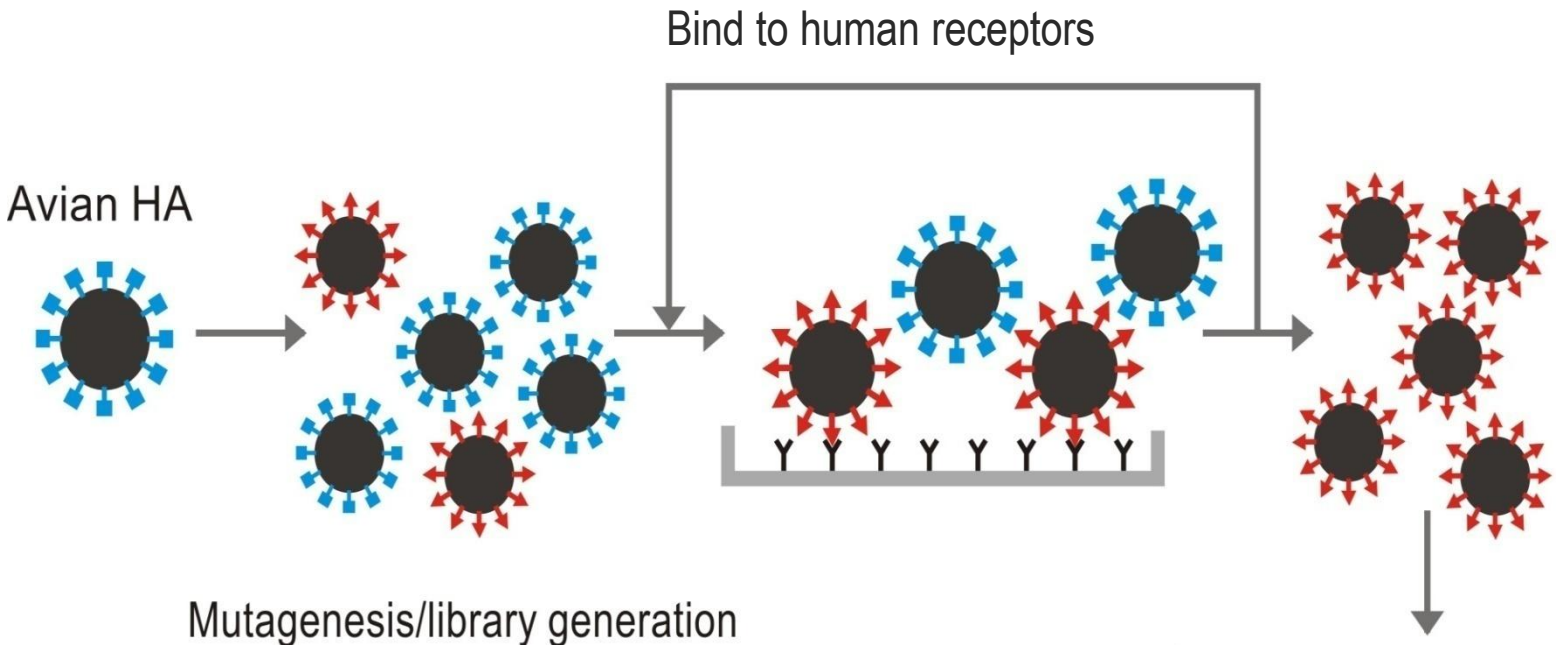


Antigenic distance



D. J. Smith et al., Science 305, 371-376 (2004)

“Pre-surveillance”: Screening viral protein libraries for pandemic risk assessment



Yoshihiro Kawaoka
University of Wisconsin-Madison

Prospects for Better Vaccines

Current vaccines → **New technologies: 5-15 years away**

Egg based vaccines
- Lmited yields
- Must predict strain shifts
- Need to revaccinate every year

Improved Adjuvants
- Some cross-protection

Recombinant protein production
- Cheaper, rapid scale-up
- Engineer for cross-protection

Distributed Manufacturing
- Worldwide access to vaccines

Transient expression in plants

Agrobacterium vector

+ Viral vector
24 hrs after infiltration

+ Viral vector
48 hrs after infiltration

Green fluorescence is indicative of GFP expression

Universal influenza vaccines

- “Conventional” universal vaccine development (e.g. M2e-based vaccines)
- Intensified epitope mapping and T-cell immune correlates of protection
- Anti-idiotypic “templating” using cross-protective monoclonal antibodies

Conclusions

- Clarify burden of disease to encourage appropriate vaccine use
- Create library of high-yield strains to prepare for vaccine production prior to pandemic
- Invest in improved vaccines/technologies to reduce costs and increase access
- Multi-use platforms can increase capacity for vaccines against pandemic influenza and other threats

Questions

BILL & MELINDA GATES foundation